

CLAIMS

We claim:

1. A targeting construct comprising:
 - 5 (a) a first polynucleotide sequence homologous to a chemokine receptor 9A gene;
 - (b) a second polynucleotide sequence homologous to the chemokine receptor 9A gene; and
 - (c) a selectable marker.
2. The targeting construct of claim 1, wherein the targeting construct further 10 comprises a screening marker.
3. A method of producing a targeting construct, the method comprising:
 - (a) providing a first polynucleotide sequence homologous to a chemokine receptor 9A gene;
 - (b) providing a second polynucleotide sequence homologous to the chemokine 15 receptor 9A;
 - (c) providing a selectable marker; and
 - (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
4. A method of producing a targeting construct, the method comprising:
 - (a) providing a polynucleotide comprising a first sequence homologous to a first region of a chemokine receptor 9A gene and a second sequence homologous to a second region of a chemokine receptor 9A gene;
 - (b) inserting a positive selection marker in between the first and second sequences to form the targeting construct.
- 25 5. A cell comprising a disruption in a chemokine receptor 9A gene.
6. The cell of claim 5, wherein the cell is a murine cell.
7. The cell of claim 6, wherein the murine cell is an embryonic stem cell.
8. A non-human transgenic animal comprising a disruption in a chemokine receptor 9A gene.
- 30 9. A cell derived from the non-human transgenic animal of claim 8.

10. A method of producing a transgenic mouse comprising a disruption in a chemokine receptor 9A gene, the method comprising:

- introducing the targeting construct of claim 1 into a cell;
- introducing the cell into a blastocyst;
- implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
- breeding the chimeric mouse to produce the transgenic mouse.

11. A method of identifying an agent that modulates the expression of a chemokine receptor 9A, the method comprising:

- providing a non-human transgenic animal comprising a disruption in a chemokine receptor 9A gene;
- administering an agent to the non-human transgenic animal; and
- determining whether the expression of chemokine receptor 9A in the non-human transgenic animal is modulated.

12. A method of identifying an agent that modulates the function of a chemokine receptor 9A, the method comprising:

- providing a non-human transgenic animal comprising a disruption in a chemokine receptor 9A gene;
- administering an agent to the non-human transgenic animal; and
- determining whether the function of the disrupted chemokine receptor 9A gene in the non-human transgenic animal is modulated.

13. A method of identifying an agent that modulates the expression of chemokine receptor 9A, the method comprising:

- providing a cell comprising a disruption in a chemokine receptor 9A gene;
- contacting the cell with an agent; and
- determining whether expression of the chemokine receptor 9A is modulated.

14. A method of identifying an agent that modulates the function of a chemokine receptor 9A gene, the method comprising:

- providing a cell comprising a disruption in a chemokine receptor 9A gene;
- contacting the cell with an agent; and

(c) determining whether the function of the chemokine receptor 9A gene is modulated.

15. The method of claim 13 or claim 14, wherein the cell is derived from the non-human transgenic animal of claim 8.

5 16. An agent identified by the method of claim 11, claim 12, claim 13, or claim 14.

17. A transgenic mouse comprising a disruption in a chemokine receptor 9A gene, wherein the transgenic mouse exhibits at least one of the following phenotypes: decreased agility, coordination, or balance relative to a wild-type mouse.

18. The transgenic mouse of claim 17, wherein decreased agility, coordination, or 10 balance is characterized by decreased performance on an accelerating rotarod.

19. The transgenic mouse of claim 17, wherein decreased agility, coordination, or balance is characterized by falling from an accelerating rotarod at lower speeds relative to a wild-type mouse.

20. A method of producing a transgenic mouse comprising a disruption in a chemokine 15 receptor 9A gene, wherein the transgenic mouse exhibits at least one of the following phenotypes: decreased agility, coordination, or balance relative to a wild-type mouse, the method comprising:

(a) introducing a chemokine receptor 9A gene targeting construct into a cell;

(b) introducing the cell into a blastocyst;

20 (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse comprising a disruption in a chemokine receptor 9A gene.

21. A transgenic mouse produced by the method of claim 20.

25 22. A cell derived from the transgenic mouse of claim 17 or claim 20.

23. A method of identifying an agent that ameliorates a phenotype associated with a disruption in a chemokine receptor 9A gene, the method comprising:

(a) administering an agent to a transgenic mouse comprising a disruption in a chemokine receptor 9A gene; and

(b) determining whether the agent ameliorates at least one of the following phenotypes: decreased agility, coordination, or balance relative to a wild-type mouse.

24. A method of identifying an agent that modulates chemokine receptor 9A expression, the method comprising:

5 (a) administering an agent to the transgenic mouse comprising a disruption in a chemokine receptor 9A gene; and

(b) determining whether the agent modulates chemokine receptor 9A expression in the transgenic mouse, wherein the agent has an effect on at least one of the following behaviors: decreased agility, coordination, or balance relative to a wild-type mouse.

10 25. A method of identifying an agent that modulates a behavior associated with a disruption in a chemokine receptor 9A gene, the method comprising:

15 (a) administering an agent to a transgenic mouse comprising a disruption in a chemokine receptor 9A gene; and

(b) determining whether the agent modulates agility, coordination, or balance of the transgenic mouse.

26. A method of identifying an agent that modulates chemokine receptor 9A gene function, the method comprising:

20 (a) providing a cell comprising a disruption in a chemokine receptor 9A gene;

(b) contacting the cell with an agent; and

(c) determining whether the agent modulates chemokine receptor 9A gene function, wherein the agent modulates a phenotype associated with a disruption in a chemokine receptor 9A gene.

25 27. The method of claim 26, wherein the phenotype comprises at least one of the following: decreased agility, coordination, or balance relative to a wild-type mouse.

28. An agent identified by the method of claim 23, claim 24, claim 25, or claim 26.

29. An agonist or antagonist of a chemokine receptor 9A receptor.

30 30. Phenotypic data associated with the transgenic mouse of claim 17 or claim 21, wherein the data is in a database.